

WHAT IS CLAIMED IS:

1 1. A method for the manufacture of a pharmaceutical tablet which upon
2 oral ingestion delivers a first drug by immediate release and a second drug by prolonged
3 release defined as a release rate into gastrointestinal fluid that is slow enough to leave at least
4 about 40% of said second drug unreleased one hour after ingestion, said method comprising:

5 (a) dispersing said second drug in a solid matrix to form a unitary body which
6 upon immersion in gastrointestinal fluid releases said second drug by prolonged
7 release;

8 (b) depositing on a surface of said unitary body a polymeric film that is
9 devoid of either said first drug or said second drug;

10 (c) depositing over said polymeric film a fluid medium comprising said first
11 drug and a liquid carrier that does not remove said polymeric film upon contact
12 therewith; and

13 (d) evaporating said liquid carrier from said fluid medium thus deposited to
14 leave a solid layer containing said first drug over said unitary body.

1 2. The method of claim 1 in which said solid matrix is a member selected
2 from the group consisting of celluloses, substituted celluloses, microcrystalline cellulose,
3 polysaccharides, substituted polysaccharides, poly(alkylene oxide)s, poly(vinyl alcohol),
4 starch, starch-based polymers, crosslinked poly(acrylic acid)s, and substituted crosslinked
5 poly(acrylic acid)s.

1 3. The method of claim 1 in which said solid matrix is a member selected
2 from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose, and
3 combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose.

1 4. The method of claim 1 in which said polymeric film is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,
3 polyvinyl alcohol, combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose,
4 and combinations of polyvinyl alcohol and poly(ethylene oxide).

1 5. The method of claim 1 in which said fluid medium comprises a liquid
2 solution of said first drug in a solvent.

1 **6.** The method of claim **1** in which said fluid medium comprises a liquid
2 solution of said first drug and a polymer in a solvent.

1 **7.** The method of claim **1** in which said fluid medium comprises a
2 suspension of said first drug in solid particle form in a liquid suspending agent.

1 **8.** The method of claim **1** in which said fluid medium comprises a
2 suspension of said first drug in solid particle form and a dispersing agent, also in solid
3 particle form, in a liquid suspending agent, said dispersing agent being a substance that
4 separates into discrete particles upon contact with gastrointestinal fluid.

1 **9.** The method of claim **1** in which said fluid medium is an aqueous
2 suspension of said first drug, and said first drug is comprised of particles having a weight-
3 averaged diameter equal to or less than 25 microns.

1 **10.** The method of claim **1** in which said fluid medium is an aqueous
2 suspension of said first drug, and said first drug is comprised of particles having a weight-
3 averaged diameter equal to or less than 10 microns.

1 **11.** The method of claim **1** in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.005:1 to about 0.2:1.

1 **12.** The method of claim **1** in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.01:1 to about 0.1:1.

1 **13.** The method of claim **1** in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.01:1 to about 0.08:1.

1 **14.** The method of claim **1** in which (b) comprises surrounding said unitary
2 body entirely with said polymeric film, and said solid layer of (d) is a shell completely
3 encasing said unitary body and polymeric film.

1 **15.** The method of claim **1** in which (b) and (c) comprise depositing said
2 polymeric film and said first drug over only a portion of the entire surface of said unitary
3 body, leaving the remainder of said unitary body exposed.

1 **16.** The method of claim **1** in which said liquid carrier of step (c) is water.

1 **17.** The method of claim 1 in which said liquid carrier of step (c) is an
2 organic solvent.

1 **18.** The method of claim 17 in which said organic solvent is a member
2 selected from the group consisting of ethanol, hexanes, chloroform, carbon tetrachloride, and
3 dimethyl sulfoxide.

1 **19.** A dosage form for delivering a first drug that is immediately releasable
2 upon ingestion and a second drug that is releasable by prolonged release defined as a release
3 rate that is slow enough to leave at least about 40% of said second drug unreleased one hour
4 after ingestion, said dosage form comprising:

5 a prolonged-release section comprising said second drug dispersed in a solid
6 matrix that releases said second drug by prolonged release upon immersion of said
7 dosage form in gastrointestinal fluid;

8 a polymeric film adhering to a surface of said prolonged-release section, said
9 polymeric film being penetrable by gastrointestinal fluid and devoid of both said first
10 drug and said second drug; and

11 an immediate-release section comprising a solid layer adhering to said
12 polymeric film, said solid layer comprising said first drug dispersed in a matrix that
13 promotes immediate release of said first drug upon immersion of said dosage form in
14 gastrointestinal fluid.

1 **20.** The dosage form of claim 19 in which said solid matrix is a member
2 selected from the group consisting of celluloses, substituted celluloses, microcrystalline
3 cellulose, polysaccharides, substituted polysaccharides, poly(alkylene oxide)s, poly(vinyl
4 alcohol), starch, starch-based polymers, crosslinked poly(acrylic acid)s, and substituted
5 crosslinked poly(acrylic acid)s.

1 **21.** The dosage form of claim 19 in which said solid matrix is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,
3 and combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose.

1 **22.** The dosage form of claim 19 in which said polymeric film is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,

3 polyvinyl alcohol, combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose,
4 and combinations of polyvinyl alcohol and poly(ethylene oxide).

1 **23.** The dosage form of claim **19** in which said solid matrix of said unitary
2 body is defined as a first solid matrix and said fluid medium comprises said first drug in
3 particle form and a second solid matrix, also in particle form, said second solid matrix being a
4 substance that separates into discrete particles upon immersion in gastrointestinal fluid.

1 **24.** The dosage form of claim **19** in which the weight ratio of said
2 polymeric film to said unitary body is from about 0.005:1 to about 0.2:1.

1 **25.** The dosage form of claim **19** in which the weight ratio of said
2 polymeric film to said unitary body is from about 0.01:1 to about 0.1:1.

1 **26.** The dosage form of claim **19** in which the weight ratio of said
2 polymeric film to said unitary body is from about 0.01:1 to about 0.08:1.

1 **27.** The dosage form of claim **19** in which said polymeric film and said
2 immediate-release section constitute a shell that fully encases said prolonged-release section.

1 **28.** The dosage form of claim **19** in which said polymeric film and said
2 immediate-release section cover a portion of the surface of said prolonged-release section,
3 leaving the remainder of said prolonged-release section exposed.

1 **29.** The dosage form of claim **19** in which one of said first and second
2 drugs is a diuretic and the other is a member selected from the group consisting of
3 angiotensin converting enzyme inhibitors and angiotensin II antagonists.

1 **30.** The dosage form of claim **29** in which said diuretic is a loop diuretic.

1 **31.** The dosage form of claim **30** in which said loop diuretic is a member
2 selected from the group consisting of furosemide, torsemide, ethacrynic acid, and
3 bumetanide.

1 **32.** The dosage form of claim **29** in which said diuretic is a thiazide
2 diuretic.

1 **33.** The dosage form of claim **34** in which said thiazide diuretic is a
2 member selected from the group consisting of chlorothiazide, bendoflumethazide,
3 hydroflumethazide, trichlorthiazide, chlorthalidone, indapamide, metolazone, quinethazone
4 and hydrochlorthiazide.

1 **34.** The dosage form of claim **29** in which said diuretic is a potassium-
2 sparing diuretic.

1 **35.** The dosage form of claim **34** in which said potassium-sparing diuretic
2 is a member selected from the group consisting of amiloride hydrochloride and triamterene.

1 **36.** The dosage form of claim **19** in which said first drug is a member
2 selected from the group consisting of lisinopril and losartan, and said second drug is a
3 diuretic.

1 **37.** The dosage form of claim **19** in which said first drug is a glitazone, and
2 said second drug is metformin hydrochloride.

1 **38.** The dosage form of claim **19** in which said first drug is pyridoxine
2 hydrochloride, and said second drug is a member selected from the group consisting of
3 atorvastatin, simvastatin, pravastatin, lovastatin, cerivastatin, rosuvastatin, and fluvastatin.

1 **39.** The dosage form of claim **19** in which said first drug is pyridoxine
2 hydrochloride, and said second drug is a member selected from the group consisting of
3 atorvastatin and simvastatin.

1 **40.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of metformin hydrochloride, vancomycin hydrochloride,
3 captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride,
4 ticlopidine hydrochloride, amoxicillin, cefuroxime axetil, cefaclor, clindamycin,
5 doxifluridine, tramadol, fluoxetine hydrochloride, ciprofloxacin hydrochloride, gancyclovir,
6 bupropion, lisinopril, cefaclor, saquinavir, ritonavir, nelfinavir, clarithromycin, azithromycin,
7 ceftazidime, cyclosporin, digoxin, paclitaxel, iron salts, topiramate, and ketoconazole.

1 **41.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of lisinopril, enalapril, captopril, fosinopril, quinapril,
3 ramipril, and benazepril.

1 **42.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of losartan, valsartan, candesartan, irbesartan, telmisartan,
3 and eprosartan.

1 **43.** The dosage form of claim **19** in which said first drug is a sulfonylurea
2 selected from the group consisting of glimepiride, glyburide, and glipizide, and said second
3 drug is metformin hydrochloride.

1 **44.** The dosage form of claim **19** in which said first drug is glimepiride and
2 said second drug is metformin hydrochloride.

1 **45.** The dosage form of claim **19** in which said first drug is glyburide and
2 said second drug is metformin hydrochloride.

1 **46.** The dosage form of claim **19** in which said first drug is glipizide and
2 said second drug is metformin hydrochloride.